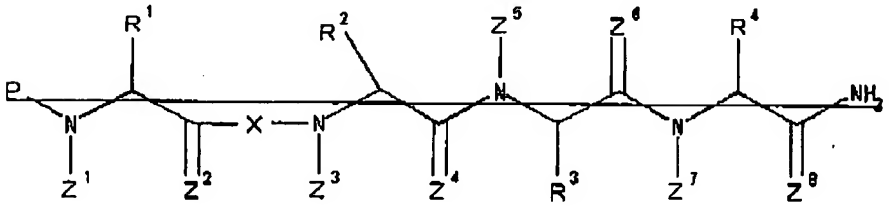
AMENDMENTS TO THE CLAIMS

Applicants respectfully request that the application be amended without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

1. (currently amended) A metastin derivative represented by formula (I):

Tyr-Asn-Trp-Asn-Ser-Phe-Gly-Leu-Arg-Tyr(Me)-NH_2



~~[wherein,~~

~~each of Z^1, Z^3, Z^5 and Z^7 represents hydrogen atom or a C_{1-3} alkyl group; each of Z^2, Z^4, Z^6 and Z^8 represents hydrogen atom, O or S;~~

~~R^1 represents (1) hydrogen atom, or (2) a C_{1-6} alkyl group optionally substituted with a substituent selected from the group consisting of an optionally substituted carbamoyl group, an optionally substituted hydroxyl group and an optionally substituted aromatic cyclic group;~~

~~R^2 represents (1) hydrogen atom or (2) a cyclic or linear C_{1-10} alkyl group, or (3) a C_{1-10} alkyl group consisting of a cyclic alkyl group and a linear alkyl group;~~

~~R^3 represents:~~

~~(1) a C_{1-6} alkyl group having an optionally substituted basic group and optionally having an additional substituent,~~

~~(2) an aralkyl group having an optionally substituted basic group and optionally having an additional substituent,~~

~~(3) a C_{1-4} alkyl group having a non-aromatic cyclic hydrocarbon group of carbon atoms not greater than 7 having an optionally substituted basic group, and optionally having an additional substituent, or,~~

~~(4) a C_{1-4} alkyl group having a non-aromatic heterocyclic group of carbon atoms not greater than 7 having an optionally substituted basic group, and optionally having an additional substituent;~~

~~R^4 represents a C_{1-4} alkyl group, which may optionally be substituted with a substituent selected from the group consisting of:~~

~~(1) an optionally substituted C_{6-12} aromatic hydrocarbon group,~~

~~(2) an optionally substituted 5- to 14-membered aromatic heterocyclic group consisting of 1 to 7 carbon atoms and hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms,~~

~~(3) an optionally substituted C_{8-14} aromatic fused ring group,~~

~~(4) an optionally substituted 5- to 14-membered aromatic fused heterocyclic group consisting of 3 to 11 carbon atoms and hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms,~~

~~(5) an optionally substituted non-aromatic cyclic hydrocarbon group having carbon atoms not greater than 7, and,~~

~~(6) an optionally substituted non-aromatic heterocyclic group having carbon atoms not greater than 7;~~

~~X represents a group shown by formula: $-NHCH(Q^1)YQ^2C(=Z^9)-$ (wherein, Q^1 represents a C_{1-4} alkyl group, which may optionally be substituted with a substituent selected from the group consisting of:~~

~~(1) an optionally substituted C_{6-12} aromatic hydrocarbon group,~~

~~(2) an optionally substituted 5- to 14-membered aromatic heterocyclic group consisting of 1 to 7 carbon atoms and hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms,~~

(3) an optionally substituted C_{8-14} aromatic fused ring group,

(4) an optionally substituted 5- to 14-membered aromatic fused heterocyclic group consisting of 3 to 11 carbon atoms and hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms,

(5) an optionally substituted non-aromatic cyclic hydrocarbon group having carbon atoms not greater than 7, and,

(6) an optionally substituted non-aromatic heterocyclic group having carbon atoms not greater than 7;

Q^2 represents (1) CH_2, which may optionally be substituted with a C_{1-4} alkyl group optionally substituted with a substituent selected from the group consisting of carbamoyl group and hydroxyl group, (2) NH, which may optionally be substituted with a C_{1-4} alkyl group optionally substituted with a substituent selected from the group consisting of carbamoyl group and hydroxyl group, or (3) O;

Y represents a group shown by formula: -CONH-, -CSNH-, $-CH_2NH-$, -NHCO-, $-CH_2O-$, $-CH_2S-$ or $-CH_2CH_2-$, which may optionally be substituted with a C_{1-6} alkyl group; and,

Z^9 represents hydrogen atom, O or S); and,

P represents:

(1) hydrogen atom;

(2) an optional amino acid residue continuously or discontinuously bound from the C-terminal end of the 1-48 amino acid sequence in the amino acid sequence represented by SEQ ID NO: 1;

(3) a group represented by formula:

J^1-J^2-$C(J^3)(Q^3)Y^1C(J^4)(Q^4)Y^2C(J^5)(Q^5)Y^3C(J^6)(Q^6)C(=Z^{10})$-

(wherein,

J^1 represents (a) hydrogen atom or (b) (i) a C_{1-15} acyl group, (ii) a C_{1-15} alkyl group, (iii) a C_{8-14} aryl group, (iv) a carbamoyl group, (v) a carboxyl group, (vi) a sulfino group, (vii) an amidino group or (viii) a glyoxyloyl group, which

~~group may optionally be substituted with (a) hydrogen atom, or (b) a substituent containing an optionally substituted cyclic group;~~

~~J^2 represents (1) NH optionally substituted with a C_{1-6} alkyl group, (2) CH_2 optionally substituted with a C_{1-6} alkyl group, (3) O or (4) S;~~

~~each of J^3 through J^6 represents hydrogen atom or a C_{1-3} alkyl group;~~

~~each of Q^3 through Q^6 represents a C_{1-4} alkyl group, which may optionally be substituted with a substituent selected from the group consisting of:~~

~~(1) an optionally substituted C_{6-12} aromatic hydrocarbon group,~~

~~(2) an optionally substituted 5- to 14-membered aromatic heterocyclic group consisting of 1 to 7 carbon atoms and hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms,~~

~~(3) an optionally substituted C_{8-14} aromatic fused ring group,~~

~~(4) an optionally substituted 5- to 14-membered aromatic fused heterocyclic group consisting of 3 to 11 carbon atoms and hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms,~~

~~(5) an optionally substituted non-aromatic cyclic hydrocarbon group having carbon atoms not greater than 7,~~

~~(6) an optionally substituted non-aromatic heterocyclic group having carbon atoms not greater than 7,~~

~~(7) an optionally substituted amino group,~~

~~(8) an optionally substituted guanidino group,~~

~~(9) an optionally substituted hydroxyl group,~~

~~(10) an optionally substituted carboxyl group,~~

~~(11) an optionally substituted carbamoyl group, and~~

~~(12) an optionally substituted sulfhydryl group,~~

~~or hydrogen atom;~~

~~J^3 and Q^3, J^4 and Q^4, J^5 and Q^5 or J^6 and Q^6 may be combined together, or, J^2 and Q^3, Y^1 and Q^4, Y^2 and Q^5, or Y^3 and Q^6 may be combined together, to form a ring;~~

~~each of Y^1 through Y^3 represents a group represented by formula:~~

~~$-CON(J^{13})-$, $-CSN(J^{13})-$, $-C(J^{14})N(J^{13})-$ or $-N(J^{13})CO-$ (wherein each of J^{13} and J^{14} represents hydrogen atom or a C_{1-3} alkyl group); and,~~

~~Z^{10} represents hydrogen atom, O or S);~~

~~(4) a group represented by formula: J^1-J^2-$C(J^7)(Q^7)Y^2C(J^8)(Q^8)Y^3C(J^9)(Q^9)C(=Z^{10})$-~~

~~(wherein,~~

~~J^1 and J^2 have the same significance as described above;~~

~~J^7 through J^9 have the same significance as J^3;~~

~~Q^7 through Q^9 have the same significance as Q^3;~~

~~Y^2 and Y^3 have the same significance as described above;~~

~~Z^{10} has the same significance as described above;~~

~~J^7 and Q^7, J^8 and Q^8 or J^9 and Q^9 may be combined together, or, J^2 and Q^7, Y^2 and Q^8 or Y^3 and Q^9 may be combined together, to form a ring);~~

~~(5) a group represented by formula:~~
~~J^1-J^2-$C(J^{10})(Q^{10})Y^3C(J^{11})(Q^{11})C(=Z^{10})$-~~

~~(wherein,~~

~~J^1 and J^2 have the same significance as described above represents;~~

~~J^{10} and J^{11} have the same significance as J^3;~~

~~Q^{10} and Q^{11} have the same significance as Q^3;~~

~~Y^3 has the same significance as described above;~~

~~Z^{10} has the same significance as described above; and,~~

~~J^{10} and Q^{10} or J^{11} and Q^{11} may be combined together, or J^2 and Q^{10} or Y^3 and Q^{11} may be combined together, to form a ring);~~

~~(6) a group represented by formula: J^1-J^2-$C(J^{12})(Q^{12})C(=Z^{10})$-~~

~~(wherein,~~

~~J^1 and J^2 have the same significance as described above;~~

~~J^{12} has the same significance as J^3;~~

~~Q^{12} has the same significance as Q^3;~~

~~Z^{10} has the same significance as described above; and,~~

~~J^{12} and Q^{12} may be combined together, or J^2 and Q^{12} may be combined together, to form a ring); or,~~

~~(7) a group represented by formula: J^1 (wherein, J^1 has the same significance as described above)] (provided that a peptide consisting of the amino acid sequence of 1-54, 2-54, 3-54, 4-54, 5-54, 6-54, 7-54, 8-54, 9-54, 10-54, 11-54, 12-54, 13-54, 14-54, 15-54, 16-54, 17-54, 18-54, 19-54, 20-54, 21-54, 22-54, 23-54, 24-54, 25-54, 26-54, 27-54, 28-54, 29-54, 30-54, 31-54, 32-54, 33-54, 34-54, 35-54, 36-54, 37-54, 38-54, 39-54, 40-54, 41-54, 42-54, 43-54, 44-54, 45-54, 46-54, 47-54, 48-54 or 48-54 in the amino acid sequence represented by SEQ ID NO: 1 is excluded), or a salt thereof.~~

2 - 6. (Cancelled)

7 - 11. (Withdrawn)

38 - 41. (Cancelled)

42 - 47. (Withdrawn)